2132.101 Examiner copy reference #3

1: Acta Diabetol. 1995 Dec;32(4):251-6.

Apolipoprotein AI-CIII-AIV genetic polymorphisms and coronary heart disease in type 2 diabetes mellitus.

Rigoli L, Raimondo G, Di Benedetto A, Romano G, Porcellini A, Campo S, Corica F, Riccardi G, Squadrito G, Cucinotta D.

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The aim of this study was to verify whether or not the increased prevalence of coronary heart disease (CHD) commonly observed in patients with type 2 diabetes mellitus is related to a genetic background involving restriction fragment length polymorphisms (RFLPs) of apolipoproteins. On the basis of a case-control design, 62 type 2 diabetic patients with CHD (confirmed by clinical history and electrocardiogram) and 62 age- and sex-matched diabetic subjects without CHD were enrolled. In each of them RFLPs of the apolipoprotein CIII gene (S1 or S2 allele) and AI promoter region (A or G allele), together with fasting plasma lipids and apolipoproteins levels, were assessed. The rare S2 allele was found significantly (P = 0.05) more frequently in patients with CHD, and its related S1S2 genotype was associated with higher plasma levels of total cholesterol (P = 0.01), triglycerides (P = 0.007) and apo B (P = 0.001) than the S1S1 genotype. The A allele was more frequent (P = 0.004) in patients without CHD and was associated with lower plasma cholesterol (P = 0.0001), low-density lipoprotein (LDL)-cholesterol (P = 0.0001) and apo B (P = 0.005). The S1/A haplotype was more frequent (P = 0.05) in patients without CHD and was associated with the lowest plasma lipid levels. These results suggest that genetic factors, related to the apo AI-CIII-AIV gene cluster, could play a role in the development of CHD in type 2 diabetic patients, probably through modification of their plasma lipid pattern.

PMID: 8750764 [PubMed - indexed for MEDLINE]

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2132.101 Examiner copy reference #4

Limits: **Publication Date from 1990 to 2000**

1: Diabetes. 1994 Dec;43(12):1485-9.

ApoA-IV polymorphism associated with myocardial infarction in obese NIDDM patients. The San Luis Valley Diabetes Study.

Rewers M, Kamboh MI, Hoag S, Shetterly SM, Ferrell RE, Hamman RF.

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Non-insulin-dependent diabetes mellitus (NIDDM) confers myocardial infarction (MI) risk unexplained by known factors. In 356 NIDDM patients and 1,087 people with normal glucose tolerance, we investigated the association between MI risk and polymorphism at codon 360 in the apolipoprotein A-IV (apoA-IV) gene. During 1984-1992, MI was diagnosed in 84 diabetic and in 106 nondiabetic people. The risk of MI did not differ by apoA-IV phenotype in nondiabetic people; however, in NIDDM patients, those with the apoA-IV 1-2 phenotype had 2.8 (95% confidence interval: 1.4-5.6) higher MI risk than those with the 1-1 phenotype, adjusting for age, gender, ethnicity, hypertension, smoking, body mass index, fat centrality, and low-density lipoprotein and high-density lipoprotein cholesterol. The risk of MI was particularly high in obese NIDDM patients with the apoA-IV 1-2 phenotype: 5.1 (2.4-11.2) times that in obese apoA-IV 1-1 NIDDM patients and 7.7 (3.6-16.7) times that in lean nondiabetic people. The effect of apoA-IV 1-2 did not appear to be a part of the insulin-resistance syndrome nor was it dependent on diabetes duration or control. One half of the excess MI risk in the diabetic population studied was explained by the apoA-IV 1-2 phenotype. These results indicate that approximately 17% of NIDDM patients have a high MI risk apoA-IV phenotype that is particularly deleterious in obese patients.

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a132.101 Examiner copy reference #5

Limits: **Publication Date from 1992 to 1992**

1: Cancer Res. 1992 May 1;52(9 Suppl):2711s-2718s.

Considerations in bringing a cancer biomarker to clinical application.

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Specific challenges face our application of emerging biomarkers to early lung cancer detection. These challenges might be considered frontiers to be bridged between established biomedical disciplines, requiring expertise often beyond the range of individual investigators. Cross-disciplinary research already has led to new appreciation of the mechanisms which underlie the phenotypic expression of the transformed cell and places within our grasp the tools which might lead to successful early lung cancer detection. Prior to the successful application of newly described markers, further cross-disciplinary research must (a) refine the selection of biologically appropriate markers, (b) validate such markers against acknowledged disease end points, (c) establish quantitative criteria for marker presence/absence, and (d) confirm marker predictive value in prospective population trials.

Publication Types:
- Review
- Review, Tutorial

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